

REMARKS

The present invention relates to novel compositions comprising a target nucleic acid bound with a binding agent, where such compositions are, *inter alia*, useful reference standards for assessing the proficiency of a nucleic acid assay. The invention further relates to methods and kits relating to the compositions.

This Supplemental Amendment follows an Interview with the Examiner and Primary Examiner Jeffrey Fredman at the U.S. Patent and Trademark Office on May 20, 2004. Applicants and the undersigned are very grateful for the kind courtesy shown to them by Drs. Strzelecka and Fredman at the Interview. An Interview Summary (Paper No. 20052004) summarizing the substance of the Interview was prepared and filed by Examiner Strzelecka noting that, among other things, "structural limitations pertaining to the nylon particles and the process of their production were discussed." Consonant with the discussions between Applicants, their representative (the undersigned), and Drs. Strzelecka and Fredman, Applicants hereby submit the instant Supplemental Amendment, which is being filed before a Final Office Action on the merits is issued in this application.

Claims 1, 3-10, 23-24, 26-30, and new claims 33-42, are pending in the present application. Claims 2, 11, and 25 were canceled previously without prejudice, and claims 12-22 and 31-32 have been canceled herein, without prejudice to the inclusion of the subject matter contained therein in any later-filed application. Further, new claims 33-42, have been added herein. Accordingly, amended claims 1, 3-10, 23, 24, 26-30, and new claims 33-42, are presently under consideration.

As more fully set forth below, these amendments and new claims are supported by the specification as filed, and no new matter has been added by way of these amendments or by the addition of new claims 33-42.

Claims 1 and 24 have been amended to recite the process by which the nylon microparticulate binding agent is produced. Ample support for these amendments is found throughout the specification as filed, including at page 51, line 1, to page 52, line 2. Thus, these amendments are fully supported by the specification as filed, and no new matter has been added by way of these amendments. Moreover, claim 3 has been amended to recite that the nylon is nylon 6/6 and claim 4 has been amended to recite that the nylon-acid solution is added dropwise to water at a rate of about two drops per second, all of which is amply supported by the

specification as filed, including, but not limited to, at page 51. Therefore, no new matter has been added by way of these amendments.

Claims 5-7, 10, 29-30, and new claims 33-35, have been amended or added, respectively, to recite that the composition is stable for at least about nine days, twenty-six days, seventy days, one-hundred three days, one-hundred fifty-one days, one-hundred fifty-nine days, and two-hundred forty-two days, at about four degrees Celsius. Support for these amendments and new claims can be found throughout the specification as filed, including, but not limited to, commencing at page 9 (description of Figures 2A through 2G), and at page 59, line 16, to page 60, line 7. Accordingly, no new matter has been added by way of these amendments or new claims reciting the stability of the composition.

Claim 27 has been added to recite that the acid used to produce the nylon microparticles of the invention encompasses hydrochloric acid. Support for this amendment is found throughout the specification as filed, including, but not limited to, page 51, citing McConway et al., 1986, J. Immunol. Methods 95:259-266. A copy of McConway et al., is attached hereto as Exhibit "A" for the Examiner's convenience. Therefore, no new matter has been added by way of this amendment.

New claims 36-40 recite various compositions of the invention comprising, *e.g.*, glycerol, alcohol (*e.g.*, ethanol and isopropyl alcohol, and the like), a chelating agent, and a buffer. Support for these claims can be found throughout the specification as filed, commencing at page 9. Therefore, no new matter has been added by way of these claims.

New claim 41 recites that the nylon binding agent has a high nucleic acid binding capacity of about 9 micrograms per milligram of solid. Support for this new claim can be found throughout the specification as filed, including, but not limited to, page 79, and Table 1. Accordingly, no new matter has been added by way of addition of claim 41.

New claim 42 merely recites that the acid is hydrochloric acid, which is amply supported throughout the specification as filed, including, but not limited to, page 51, citing McConway et al. Therefore, no new matter has been added by addition of this claim.

In sum, the specification as filed provides ample support for the claim amendments and new claims set forth herein. Therefore, the amendments and new claims do not add any new matter.

Applicants respectfully submit that the amendments and new claims provided herein overcome each rejection set forth in the Office Action mailed September 29, 2003 (Paper No. 3) for the following reasons.

Rejection of claims 1 and 8-10, pursuant to 35 U.S.C. § 102(b)

Claims 1 and 8-10 stand rejected under 35 U.S.C. § 102(b), as being anticipated by Hayatsu et al. (1997, Chem. Pharm. Bull. 45:1363-1368). The Examiner reasons that Hayatsu teaches genomic DNA (calf thymus and salmon testis) bound to chitosan thereby anticipating the reference nucleic acid standard of claim 1, and claims depending therefrom. Applicants respectfully submit that Hayatsu does not anticipate the present invention since the claims have been amended, and new claims have been added, which do not recite chitosan. Accordingly, rejection of the claims as amended, as well as new claims 33-42, is now moot. Therefore, Hayatsu, which does not describe each and every element of the claims as now amended, or of new claims 33-42, does not anticipate the present invention and the rejection under 35 U.S.C. § 102(b) should be reconsidered and withdrawn.

Rejection of claims 1 and 8-10, pursuant to 35 U.S.C. § 102(b)

Previously, claims 1 and 8-10 were rejected under 35 U.S.C. § 102(b), as being anticipated by Kariko et al. (1998, Biochim. Biophys. Acta 1369:320-334). The Examiner is of the opinion that Kariko teaches plasmid DNA (and RNA) bound to a cationic liposome and thereby anticipating the present invention. Applicants respectfully submit that Kariko does not anticipate the present invention because the claims, as amended, and the new claims added herein, do not recite liposomes. Because Kariko et al., has nothing whatsoever to do with the nylon microparticles of the present invention as recited in the claims currently under consideration, this reference cannot anticipate the present invention. Therefore, Applicants respectfully contend that Kariko does not anticipate the present invention as recited in the amended claims herein, and in new claims 33-42 added herein, and the rejection under 35 U.S.C. § 102(b) should be reconsidered and withdrawn.

Rejection of claims 1, 3, 5 and 7-10, pursuant to 35 U.S.C. § 102(b)

Claims 1, 3, 5, and 7-10 stand rejected under 35 U.S.C. §102(b), as being anticipated by Boom et al. (EP 0819696 A2). The Examiner is of the opinion that Boom teaches DNA bound to silicon dioxide particles, a nylon filter, diatomaceous earth, particles with 70% ethanol. Applicants respectfully submit that Boom does not anticipate the present invention because the reference does not describe the nylon microparticles as required by the claims as amended herein, and by new claims 33-42 added herein. Thus, Boom et al., does not anticipate the present invention and the rejection under 35 U.S.C. §102(b) should be reconsidered and withdrawn.

Rejection of claim 4, pursuant to 35 U.S.C. § 103(a)

The Examiner has rejected claim 4 under 35 U.S.C. §103(a) as being *prima facie* obvious over Boom et al. and Holmberg (EP 0514513 B1). Specifically, the Examiner is of the opinion that Boom teaches DNA bound to polystyrene particles and that Holmberg teaches binding of oligonucleotides to polystyrene solid support derivatized with an amino group. Applicants respectfully submit that Boom et al. and Holmberg et al. cannot render claim 4 *prima facie* obvious under 35 U.S.C. §103(a) because the combination of these references does not teach or suggest the nylon microparticles of the invention. Nor would there have been any motivation to combine these references to produce or use the microparticles, and there would not have been any reasonable expectation that combining these references would produce the microparticles. Therefore, the combination of Boom and Holmberg cannot render claim 4, as amended, *prima facie* obvious under 35 U.S.C. §103(a), and the rejection should be reconsidered and withdrawn.

Rejection of claim 6, pursuant to 35 U.S.C. § 103(a)

The Examiner has rejected claim 6 under 35 U.S.C. §103(a) as being *prima facie* obvious over Boom, *supra*, and Matsui et al. (2001, Chemistry Eur. J. 7:1555-1560). As discussed elsewhere herein, the Examiner is of the opinion that Boom teaches DNA bound to silicon dioxide particles, a nylon filter, diatomaceous earth, particles with 70% ethanol. The Examiner also asserts that Matsui et al. teaches the binding of DNA to low alumina zeolites. Therefore, the Examiner reasons that it would have been *prima facie* obvious to combine the teachings of Boom et al. and Matsui et al. to arrive at the present invention as recited in claim 6.

Applicants respectfully submit that Boom et al. and Matsui et al. cannot render claim 6, as amended, *prima facie* obvious under 35 U.S.C. §103(a) because the combination of these references does not teach or suggest the nylon microparticles now recited in claim 6 as amended. Nor would there have been any motivation to combine these references to produce the composition recited in amended claim 6, nor any reasonable expectation that doing so would arrive at the composition recited in the claim as it now reads.

For these reasons, the combination of Boom et al., and Matsui et al., cannot render claim 6, as amended, *prima facie* obvious under 35 U.S.C. §103(a), and this rejection should be reconsidered and withdrawn.

Rejection of claim 23, 24, 26, 28 and 30-32, pursuant to 35 U.S.C. § 103(a)

The Examiner has rejected claims 23, 24, 26, 28 and 30-32 under 35 U.S.C. §103(a) as being rendered *prima facie* obvious over Boom et al. in view of the Stratagene catalog. As discussed elsewhere herein, the Examiner is of the opinion that Boom teaches DNA bound to silicon dioxide particles, a nylon filter, diatomaceous earth, particles with 70% ethanol and the Stratagene catalog teaches kits, thereby rendering obvious kits comprising the reference nucleic acid of Applicants' invention. Applicants respectfully submit that Boom et al. in view of the Stratagene catalog does not render the invention *prima facie* obvious because the combination of Boom et al., and the Stratagene catalog do not teach or suggest the nylon microparticles as recited in claims 23, 24, 26, 28, and 30 as amended. (Claims 31 and 32 having been canceled herein, the rejection of these claims is now moot.) Furthermore, there would have been no motivation to combine Boom et al., and the Stratagene catalog to arrive at the kits recited in claims 23, 24, 26, 28, and 30, nor could there have been any reasonable expectation of success in combining these references since there is no teaching or suggesting as to the nylon microparticles, among other things. Therefore, Boom, in view of the Stratagene catalog, cannot render the claims *prima facie* obvious and this rejection under 35 U.S.C. § 103(a) should be reconsidered and withdrawn.

Rejection of claim 27 pursuant to 35 U.S.C. § 103(a)

The Examiner has rejected claim 27 under 35 U.S.C. §103(a) as being *prima facie* obvious over Boom et al. in view of Stratagene Catalog and Holmberg. Specifically, the

Examiner is of the opinion that Boom teaches isolated nucleic acid bound to polystyrene particles, and Holmberg teaches binding of oligonucleotides to polystyrene solid support derivatized with an amino group. Therefore, the Examiner reasons that it would have been *prima facie* obvious for one skilled in the art to combine the teachings of these references to arrive at the present invention as recited in claim 27. Applicants respectfully submit that the combination of these references cannot render claim 27 *prima facie* obvious since they have nothing whatsoever to do with the nylon microparticles now recited in amended claim 27. Thus, there would have been no motivation to combine these references, nor any reasonable expectation of success in doing so, to arrive at the invention as recited in claim 27 as amended. Therefore, Boom, in view of Holmberg and the Stratagene catalog, cannot render claim 27 as amended *prima facie* obvious, and this rejection under 35 U.S.C. § 103(a) should be reconsidered and withdrawn.

Rejection of claim 29 pursuant to 35 U.S.C. § 103(a)

The Examiner has rejected claim 29 under 35 U.S.C. § 103(a) as being *prima facie* obvious over Boom et al. in view of Stratagene Catalog and Matsui et al. Specifically, the Examiner is of the opinion that Boom teaches isolated nucleic acid bound to polystyrene particles, and Matsui teaches adsorption (binding) of nucleic acids to low alumina zeolites. Therefore, the Examiner reasons that it would have been *prima facie* obvious for one skilled in the art to combine the teachings of the reference to arrive at the present invention as recited in claim 29. Applicants respectfully submit that the combination of the references do not render claim 29 as amended *prima facie* obvious in that, as previously set forth elsewhere herein, the combination of these references does not teach or suggest the nylon microparticles now recited in amended claim 29. Further, there would have been no motivation to combine these references to arrive at the invention as recited in claim 29 as amended, nor could there have been any reasonable expectation of success in such combination.

Therefore, Boom, in view of Matsui and the Stratagene catalog, cannot render claim 29, as amended, *prima facie* obvious, and this rejection under 35 U.S.C. § 103(a) should be reconsidered and withdrawn.

Summary

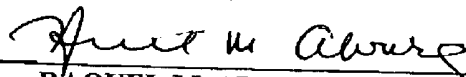
Applicants respectfully submit that each objection and rejection of the Examiner to the claims of the present application has been either overcome or is now inapplicable, and that each of claims 1, 3-10, 23, 24, 26-30, and new claims 33-42, is in condition for allowance. Reconsideration and allowance of each of these claims are respectfully requested at the earliest possible date.

Respectfully submitted,

CLARK RUNDELL *ET AL.*

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Date

By:



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Enclosure: Exhibit "A" (copy of McConway et al., 1986, J. Immunol. Methods 95:259-266)